PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING

To:
Darae Patent Firm

10th Floor, KIPS, 647-9 Yeoksam-dong, Kangnam-ku, Seoul
135-980, Republic of korea

PCT

WRITTEN OPINION

(PCT Rule 66)

Date of mailing *(day/month/year)*	06 AUGUST 2004 (06.08.2004)
Applicant's or agent's file reference 02PP174	**REPLY DUE** within 2 months from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/KR2002/001875	**08 OCTOBER 2002 (08.10.2002)**	14 AUGUST 2002 (14.08.2002)

International Patent Classification (IPC) or both national classification and IPC

IPC7 A61K 31/164

Applicant

KIM, Tae-Yoon et al

1. This written opinion is the first (first,etc.) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	[X]	Basis of the opinion
II	[ ]	Priority
III	[X]	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	[ ]	Lack of unity of invention
V	[X]	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	[ ]	Certain documents cited
VII	[ ]	Certain defects in the international application
VIII	[X]	Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

When ? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d)

How ? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3
For the form and the language of the amendments, see Rules 66.8 and 66.9

Also For an additional opportunity to submit amendments, see Rule 66.4
For an examiner's obligation to consider amendments and/or arguments, seeRule 66.4bis
For an informal communication with the examiner, see Rule 66.6

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 04 DECEMBER 2004 (04.12.2004)

Name and mailing address of the IPEA/KR Korean Intellectual Property Office 920 Dunsan-dong, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140	Authorized officer KIM, Hee Jin Telephone No. 82-42-481-5412

Form PCT/IPEA/408 (cover sheet) (July 1998)

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International application No.
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I. Basis of the opinion

1. With regard to the elements of the international application:*

[X] the international application as originally filed

[ ] the description:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

[ ] the claims:
pages _____, as originally filed
pages _____, as amended (together with any statment) under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

[ ] the drawings:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

[ ] the sequence listing part of the description:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language English which is

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[X] the language of publication of the international application(under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

[ ] contained inthe international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international applicationas as filed has been furinshed.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages _____

[ ] the claims, Nos. _____

[ ] the drawings,sheet/fig _____

5. [ ] This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box(Rule 70.2(c)).

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."*

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☐ claims Nos. _____

because:

☒ the said international application, or the said claims Nos. 15-19
relate to the following subject matter which does not require an international preliminary examination *(specify)*:

The subject-matter of claims 15-19 does not require an international preliminary examination with respect ot industrial applicability as it is directed to a method for treatment of the human or animal body by therapy(Article 34(4)(a)(i), Rule 67.1(iv)).

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____
are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequencelisting to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furniahed or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

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V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-14	YES
	Claims		NO
Inventive step (IS)	Claims	3,10	YES
	Claims	1-2, 4-9, 11-14	NO
Industrial applicability (IA)	Claims	1-14	YES
	Claims		NO

2. Citations and explanations

D1: FEBS LETTERS, vol.499, pp.82-6

D2: Journal of Neurochemistry, vol.75, no.3, pp.1053-9(not cited in the search report)

D3: KR 1044801 A

D4: US 6403111

D5: EP667853 B

D6: US 6372236

D7: Cellular and molecular biology, 2000, vol.46, no.1, pp.111-9(not cited in the search report)

본원발명은 피토스핑고신 유도체를 함유하는 아폽토시스 유도용 약학조성물, 화장료 조성물에 관한 발명이다.

D1에는 피토스핑고신과 N-아세틸피토스핑고신이 chinese hamster ovary(CHO) cell에 대해서 세포독성이 있으며 또한 phospholipase D의 활성을 억제한다고 기재되어 있다.

D2에는 phospholipase D의 활성을 억제하면 H202로 유도된 아폽토시스가 현저하게 증가된다고 기재되어 있다.

D3에는 피부노화 억제제로서 유용한 아세틸화 N-아세틸파이토스핑고신 레틴아미드 유도체가 기재되어 있다.

D4에는 물에 대한 용해도가 낮은 피토스핑고신을 높은 농도로 함유하고 있는 수용액을 제조하는 방법에 대해 기재되어 있다.

D5에는 피토스핑고신을 가지는 세라마이드의 합성방법과 이를 함유하는 화장용조성물에 대해 기재되어 있다.

D6에는 피토스핑고신을 함유하는 skin care composition에 대해 기재되어 있다.

D7에는 비타민D3, 칼시포트리올 등이 케라티노사이트에 아폽토시스를 유발한다고 기재되어 있다.

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VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

본원발명의 명세서에 기재된 "CLA-phytosphingosine(CLA-PS)"라는 용어는 당업계에 통용되지 않고 그 정의도 기재되어 있지 않아 불명확합니다.

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Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of:

1. Novelty
상기에 기재된 선행기술들에 피토스핑고신 유도체를 유효성분으로 함유하는 아폽토시스 유도용 조성물에 대한 기재가 없으므로 본원발명은 신규하다.

2. Inventive Step
D1이 가장 가까운 선행기술로 인정된다.
(1) claims 1,2,8,9
본원발명과 D1을 비교해보면 피토스핑고신, N-아세틸피토스핑고신이 세포독성을 가진다는 점에서 동일하나 D1에는 피토스핑고신, N-아세틸피토스핑고신이 phospholipase D의 활성을 억제시킨다고 기재되어 있을 뿐 아폽토시스를 유발하는 mechanism으로 인한 것이라고 기재되어 있지는 아니하다는 점에서 본원발명과 차이점이 있다. 그러나, D2에 phospholipase D의 활성을 억제하면 아폽토시스가 증가한다고 기재되어 있어 D2로부터 피토스핑고신, N-아세틸피토스핑고신이 아폽토시스를 유발시킨다는 것을 용이하게 도출할 수 있다. 따라서, 본원발명의 특허청구범위 1,2,8,9항은 당업자가 D1,D2로부터 용이하게 발명할 수 있는 것으로 진보성이 없다고 인정된다.
(2) claims 4-7, 11-14
본원발명의 특허청구범위 4항 내지 7항 및 11항 내지 14항은 아폽토시스 활성 유도에 의해 치료 가능한 질환을 한정하고 있으나 이러한 질환들이 아폽토시스를 유도하면 효과적으로 치료된다는 사실은 본원발명의 description에서도 기재되어 있듯이 공지의 사실이므로 피토스핑고신 유도체를 이들 질환에 적용하는 데 곤란성이 있다고 볼 수 없으므로 claims 4-7, 11-14항도 D1,D2에 대해서 진보성이 없다고 인정된다.

(3) claims 3,10
본원발명의 특허청구범위 제3항 및 10항은 피토스핑고신 유도체에 비타민 D3 또는 칼시포트리올을 추가로 함유하는 조성물에 관한 발명이나 D7에 비타민 D3, 칼시포트리올 등이 케라티노사이트에 아폽토시스를 유발한다고 기재되어 있어 당업자라면 D1,D7로부터 claims 3,10을 구성하는데 곤란성이 있다고 볼 수 없으나 이들을 병용투여하였을 때 현저한 상승효과가 있다고 인정되므로(표4참고), 상기 청구항들은 진보성이 인정된다.

3. Industrial Applicability
본원발명의 특허청구범위 제1항 내지 제14항은 산업상 이용가능성이 있다.